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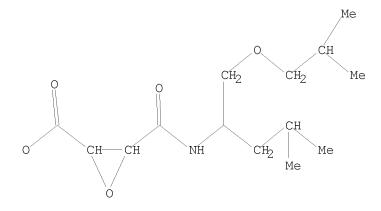
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L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN GI

AΒ Novel epoxysuccinamide derivs. (3-carboxyoxirane-2-carboxamides) represented by general formula (I) or physiol. acceptable salts thereof [wherein R1 and R3 are each H, alkyl, alkenyl, alkynyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; R2 is alkyl, alkenyl, alkynyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; X is O or NR4 (wherein R4 is H, alkyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group); Y1 is OR5, SR6 or NR7R8 (wherein R5, R6 and R7 are each H, alkyl, aryl, aralkyl, acyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; and R8 is the same as defined as to R4); and Y2 is H or alkyl, or alternatively Y1 and Y2 may be united to form =0, =S, =N-R9 or =N-OR10 (wherein R9 and R10 are each the same as defined as to R4), with the proviso that the alkyl, aryl and heterocyclic groups defined as to R5 to R10 may each have one or more specific substituents and that the groups defined as to R1 to R10 and Y2 are each specified in the number of carbon atoms] are prepared These compds. inhibit bone absorption and activity of cathepsin L and B (cysteine protease) and are useful for the treatment of bone diseases such as osteoporosis, malignant hypercalcemia, and Paget's disease of bone, arthritis deformans and chronic articular rheumatism accompanied by unusual exasperation of cathepsin B and L activity, and muscular dystrophy and muscular atrophy related to cathepsin B and L. Thus, (2S,3S)-3-ethoxycarbonyloxirane-2-carboxylic acid was condensed with

 $(S)-1-[(R)-\alpha-methoxybenzyl]-3-methylbutylamine using$ N-hydroxysuccinimide and DCC in EtOAc at room temperature overnight to give the title compound (II). II at 15 mg/kg p.o. lowered serum calcium by 20.4% in 1999:184251 CAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 130:223163 TITLE: Preparation of epoxysuccinamide derivatives for treatment of bone diseases and arthritis INVENTOR(S): Nomura, Yutaka; Takahashi, Toshihiro; Yoshino, Yasushi; Nishioka, Koichiro PATENT ASSIGNEE(S): Nippon Chemiphar Co., Ltd., Japan PCT Int. Appl., 86 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: Japanese FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION: PATENT NO. APPLICATION NO. KIND DATE DATE ____ _____ _____ _____ WO 9911640 A1 19990311 WO 1998-JP3983 19980904 <--W: AU, CA, CN, JP, KR, RU, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9889978 19990322 AU 1998-89978 19980904 <--Α EP 1022276 20000726 EP 1998-941728 19980904 <--Α1 20030528 EP 1022276 В1 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI AT 241607 Т 20030615 AT 1998-941728 19980904 <--EP 1342720 A2 20030910 EP 2003-11154 19980904 20040211 EP 1342720 АЗ R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY PT 1022276 20031031 PT 1998-941728 19980904 ES 2201524 Т3 20040316 ES 1998-941728 19980904 US 6387908 В1 20020514 US 2000-508026 20000505 <--US 20020091131 A1 20020711 US 2002-42994 20020108 <--US 6689785 В2 20040210 JP 1997-257538 A 19970904 EP 1998-941728 A3 19980904 PRIORITY APPLN. INFO.: WO 1998-JP3983 W 19980904 US 2000-508026 A3 20000505 OTHER SOURCE(S): MARPAT 130:223163 221144-15-6P 221144-16-7P 221144-17-8P 221144-18-9P 221144-19-0P 221144-20-3P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of epoxysuccinamide derivs. as bone absorption inhibitors and cathepsin B and L inhibitors for treatment of bone diseases and arthritis)

CN

221144-15-6 CAPLUS

RN

2-Oxiranecarboxylic acid, 3-[[(1S)-3-methyl-1-[(2-methyl-1)-1]]]methylpropoxy)methyl]butyl]amino]carbonyl]-, 1-methylethyl ester, (2S,3S)-(CA INDEX NAME)

Absolute stereochemistry.

RN 221144-16-7 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 221144-17-8 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, cyclohexyl ester, (2S,3S)-(CA INDEX NAME)

Absolute stereochemistry.

RN 221144-18-9 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, phenyl ester, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 221144-19-0 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[(1S)-3-methyl-1-[(2-methyl-1)-[(2-methyl-1)-[(2-met

methylpropoxy)methyl]butyl]amino]carbonyl]-, 4-(1,1-dimethylethyl)phenyl
ester, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 221144-20-3 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, sodium salt (1:1), (2S,3S)-(CA INDEX NAME)

Absolute stereochemistry.

Na

REFERENCE COUNT:

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